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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/960,315	09/24/2001	Robert W. Wannemacher	12694/P66821US2 (RIID99-2	6514

53502 7590 04/20/2006

OFFICE OF THE STAFF JUDGE ADVOCATE (SKS)
U.S. ARMY MED. RESEARCH & MATERIAL COMMAND
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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,315	WANNEMACHER ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,19,21-25,40 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,19,21-25,40 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/523,271; which claims the benefit of the filing date of provisional application 60/124,283..

Claims 1-16, 19, 20, 26-39 and 41-43 have been canceled.

Claims 17, 18, 21-25, 40 and 44-46 are currently pending and are the subject of examination in the present Office Action.

Withdrawal from Issue

It is noted that the instant application was previously indicated as being allowed on June 24, 2005. However, further review of the claimed invention has necessitated withdrawal of the application from allowance. The previous ground of rejection has been modified in view of this further review and is present ed infra as a new ground of rejection.

Accordingly, the present NEW GROUND of rejection necessitates this NON-FINAL Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 17, 18, 21-24, 40 and 44-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "inducing a mean ELISA titer" using the exemplified ELISA assay, does not reasonably provide enablement for "inducing a mean ELISA titer" by any other ELISA assay. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to inducing a mean ELISA titer of about 1 x 10^2 mg/ml or more against ricin toxin in a subject. However, the claim does not recite the conditions under which the ELISA assay for determining the titer is conducted. The disclosure provides only a single example of an ELISA assay that can consistently determine the requisite antibody titer in a subject or between subjects. The ability of an ELISA assay to reproducibly determine an antiserum titer is dependent upon a number of factors including, but not limited to, the nature of the solid phase, the nature of the antigen used, the manner in which the antigen is coupled to/coated upon the solid phase, the incubation buffer/conditions, the properties of the secondary detection antibody used and the nature of the labeling enzyme used and the nature of the substrate used. Other than by the method exemplified in the specification, the artisan would otherwise not know how to determine whether or not the antibody titer in the subject meets the criteria of having "a mean ELISA titer of about 1 x 10^2 mg/ml or more against ricin toxin."

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 17, 18, 21-24, 40 and 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is ambiguous and unclear for reciting, "inducing a mean ELISA titer" in the claim without recitation of the conditions under which the ELISA titer is obtained. The phrase is indefinite because the titer measured depends upon the reagents used and the conditions for conducting the ELISA. ELISA assay sensitivity (and thus measured titer) is affected by at least all of the following:

- The nature of the solid phase.
- The nature of the antigen used.
- The manner in which the antigen is coupled to/coated upon the solid phase.
- The incubation buffer/conditions.
- The properties of the secondary detection antibody used (e.g., its binding avidity).
- The nature of the labeling enzyme used and the nature of the substrate used (e.g., some substrates give a more sensitive signal).

Thus, one can get different titers for the same antiserum depending upon how the ELISA test is conducted.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 17, 18, 21-25, 40 and 44-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Thorpe et al (Eur. J. Biochem. [1985] 147:197-206; AV on form PTO-1449).

Applicant's claimed method consists of a single step, which is the administration an amount of chemically deglycosylated ricin A chain, wherein the ricin B-chain has been removed. The recitation in the claim of inducing a particular titer of anti-ricin antibodies is merely a characterization of the result of practicing the method and does not limit the method itself.

Thorpe teaches the deglycosylation of ricin A chain with sodium metaperiiodate and cyanoborohydride at a pH of 3.5 at 4°C (page 198, second column in particular). Thorpe teaches that the level of deglycosylation was dependent upon the incubation time and a maximum of 13 out of the total 18 mannose residues were destroyed (Abstract in particular). Thorpe teaches in Figures 2 and 3 that after 60 minutes of $IO_4^-/CNBH_3$ treatment (specifically recited in instant claim 18) about 50% of the mannose is destroyed and Figure 2 further shows that most fucose is destroyed. Thorpe further teaches that the 60-minute composition was administered to animals (Table 2 in particular) and that "the duration of treatment of ricin with $IO_4^-/CNBH_3$ that gives maximal avoidance of reticuloendothelial recognition with least reduction in cytotoxic activity is 60 min under the conditions used in this study" (page 205, last paragraph of column 1 in particular). Thorpe teaches the administration of 20 μg/kg to rat subjects (Table 3 in particular). Thorpe teaches that ricin immunotoxins prepared in this manner to be administered to subjects can be just the A chain of the ricin molecule (page 205, last paragraph of column 1 in particular; emphasis added to show difference from previous ground of rejection). While Thorpe is silent regarding the production of ricin-reactive antibodies in the treated subject, Thorpe teaches administration of ricin A chain that has been incompletely deglycosylated in the same manner as that disclosed in the instant specification (page 7, line 17 to page 8, line 5 for example) within the claimed range of administration. Accordingly, the production of antibodies to ricin is inherent to the method of incompletely deglycosylated ricin A chain administration taught by Thorpe. Furthermore, given the indefiniteness concerning titer in claim 17 and as addressed in paragraph 2 *supra*, the recited titer would have inherently

been achieved by the artisan using the method of Thorpe based solely upon manipulation of the ELISA conditions used.

The prior art teaching anticipates the claimed invention.

Conclusion

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
April 6, 2006

David a Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 / 644